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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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In re Application of:

Robert E. GARFIELD et al. Examiner: H. Lilling

Serial No.: 09/121,849 Group Art Unit: 1651

Filed: July 24, 1998

For: TREATMENT OF PREECLAMPSIA TOXEMIA AND PRETERM LABOR WITH COMBINATION OF PROGESTATIONAL AGENT AND A NITRIC OXIDE SYNTHASE SUBSTRATE AND/OR DONOR

Assistant Commissioner for Patents
Washington, D.C. 20231

I hereby certify that this correspondence is being deposited with the U.S. Postal Services as First Class Mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231 on: August 19, 2002
Name: CARLA HENTER
Signature:
Date: August 19, 2002

REPLY BRIEF

Sir.

In response to the Examiner's Answer dated June 18, 2002, please consider the following remarks.

REMARKS

The Examiner's Answer on page 10 alleged that "there are several examples demonstrating various combinations of nitric oxide precursors or donors with various other agents that demonstrates success which agents are considered to be functionally equivalent" to compounds a) and c) of the present invention. The Examiner's answer does not specify which prior art examples demonstrate various combinations, neither to what they specifically teach, nor to which claimed element the alleged other agents are considered to be functionally equivalent. Applicants disagree with the allegations.

Contrary to the allegations, the prior art examples indeed teach away from the present invention. A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *See W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) and M.P.E.P. 2141.02. The examples of Harrison et al., US 5,508,045 are discussed next.

Example 1 teaches that active labor was induced in monkeys by progestins alone.

Example 2 tests the inhibitory activity of S-Nitroso-N-Acetylpenicillanimine alone on Monkeys.

Example 3 tests the inhibitory activity of papaverine hydrochloride, zaprinast and amrinone, each individually.

Example 4 tests nitric oxide synthase activity in pregnant rat uterus.

Example 5 tests the effect of nitroglycerin alone on active labor in sheep.

Example 6 tests the effect of nitroglycerin alone on preterm labor in human patients after hysterotomy. The example teaches that "other than bolus doses of terbutaline used in one case, no other intraoperative tocolytic was required." See column 31, lines 64-65. The specification on column 21, lines 39 to 50 teaches that terbutaline is a β-adrenergic agonist. Compounds listed as β-adrenergic agonist, i.e., functional equivalents, are "epinephrin, isoproterenol isopropylnorepinephrine), p-hydroxyphenylisopropylarterenol), isoxsuprine, orciprenaline, (1-(3,5-dihydroxyphenyl)-2-isopropylaminoethanol sulfate, salbutamol, terbutaline, analogues thereof, and other agents known in the art." None of these correspond to compounds a) or c) of the presently claimed invention. Thus, this example, contrary to the allegation, does not teach or suggest a composition as claimed.

Furthermore, this example teaches that other than bolus doses of terbutaline used in one case, no other intraoperative tocolytic was required. Thus, this example, contrary to the allegations, in effect teaches away from the administration of a composition containing three different cotolytic agents.

Example 7 teaches eight human patient cases wherein nitroglycerin is administered to each patient. Some of the patients also received individual doses of terbutaline (discussed in conjunction with example 6) and individual doses of indocin. The specification teaches that indocin is a postoperative cotolyst. Compounds listed as postoperative cotolyst, i.e., functional equivalents, are magnesium sulfamate, betamimetics, and indocin. See specification on column 19, lines 8-9. None of these correspond to compounds a) or c) of the presently claimed invention. Thus, this example, contrary to the allegation, does not teach or suggest a composition as claimed.

Example 8 tests pharmacologic manipulation of isolated monkey uterine muscle strips by the test drugs: "L-arginine, L-NMA, L-NA, NMDA, VIP, rat cGRP, SNAP, methylene blue, M&B 22948, Rolipram, and 8-bromo-cGMP."

None of the examples teaches or suggests the presently claimed invention.

The Examiner's Answer on page 7 and 8 alleges that the prior art would have motivated one to employ any combination of the claimed "mixture" since the agents are functionally equivalent behaving the same manner to treat the same symptoms. Applicants however disagree. Neither does the prior art teach that the agents are all functionally equivalent, see discussion above, nor that they behave in the same manner to treat the same symptoms. The reference teaches, for example, lists of postoperative cotolyts, see column 19, lines 8-9, β-adrenergic agonists, see column 21, lines 39-50, oxytocin antagonists, column 22, lines 28-31, prostaglandin synthesis inhibitors, see column 21, lines 51-62, magnesium salts, column 21, lines 63-67, calcium transport blockers, see column 22, lines 1-11, ethanol, column 22, lines 18-21, phosphodiesterase inhibitors, column 22-27, and progestins, column 22, lines 12-21. Each of these genuses of cotolysts has a different function and behaves differently. For example, β-adrenergic agonists are compounds capable of stimulating one or more types of β-adrenergic receptors, prostaglandin synthesis inhibitors are compounds which inhibit any step or steps in the series of enzymatic reactions involved in the synthesis of prostaglandins, and calcium transport blockers are capable of reducing the importation of extracellular calcium. See column 21, line 26 to column, 22, line 31. These cotolytic agents are thus not taught to be functionally equivalent, nor are they taught to behave in the same manner to treat the same symptoms. Thus, the allegations to the contrary are without basis.

Contrary to the allegations on page 11 of the Examiner's Answer to the effect that there is an exceptionally limited number of specific agents disclosed in the reference coupled with motivation for the selection of the specific agents, the disclosure of the reference teaches numerous broad classes along with numerous exemplified species of cotolytic agents throughout the disclosure, and especially on columns 21 and 22, encompassing thousands of compounds and even more possible combinations. The reference does not provide motivation to the combination of any number of mixtures. There is not an exceptionally limited number of agents as alleged by the Examiner's Answer. The fact scenario of *In re Baird*, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994), is fully applicable in the present situation contrary to the assertions in the Examiner's Answer. The disclosure of the reference is broad, encompassing thousands of possibilities without motivation toward the selection of any species in accord with the presently claimed invention.

Reversal of the rejection is respectfully requested.

The Commissioner is hereby authorized to credit or debit counsel's Deposit Account No. 13-3402 for and under- or overpayment of fees.

Respectfully submitted,

Csaba Henter, Reg. No. 50,908
Anthony J. Zelano, Reg. No. 27,969
Attorney/Agent for Appellants

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza I
2200 Clarendon Boulevard
Suite 1400
Arlington, VA 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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I hereby certify that this correspondence is being deposited with the U.S. Postal Services as First Class Mail in an envelope addressed to: Assistant Commissioner For Patents. Washington, D.C. 20231 on: August 19, 2002
Name: CSABA HENTER
Signature:
Date: August 19, 2002